

IN THE CLAIMS

Please amend the claims as follows:

Claims 1-94 (Cancelled).

95. (Currently Amended) A method for obtaining human T cells with enhanced replicative function and cytokine secretion comprising

inoculating a culture with human T-cells;

culturing the human T cells under physiologically acceptable liquid culture conditions,

said conditions including replacement of a liquid culture medium at rate of from 50% to 100% daily replacement for a cell density of from 1×10^4 to 1×10^7 cells per ml of culture for more than one day and for a time sufficient to obtain human T-cells with enhanced replicative function and cytokine secretion,

wherein said enhanced replicative function and cytokine secretion is relative to the replicative function and cytokine secretion of the human T-cells that are cultured in a static or hemi-depletion culture, and

wherein the cell density of the T-cells is not substantially reduced or adjusted at any time during the culturing while maintaining a constant culture volume.

96. (Previously Presented) The method of claim 95, wherein the culture medium is continuously perfused at a ramped rate proportional to the lactate concentration and/or cell density to replace the culture medium without substantial dilution of the cell density.

97. (Previously Presented) The method of claim 95, wherein the human T-cells are cultured for at least 2 days.

98. (Previously Presented) The method of claim 95, wherein the culture medium contains at least 1 growth factor which stimulates the proliferation of the human T-cells.

Claims 99-113 (cancelled).

114. (New): The method of claim 95, wherein replacement of said medium comprises perfusing fresh medium through at least part of the mass of said human T-cells.

115. (New): The method of claim 95, wherein said medium comprises animal or human sera or plasma.

116. (New): The method of claim 95, comprising maintaining glucose concentration in said medium in the range of from 5 to 20 mM, lactate concentration in said medium below about 35 mM, glutamine concentration in said medium in the range of from 1 to 3 mM, and ammonia concentration in said medium below 2.4 mM.

117. (New): The method of claim 95, further comprising removing nonadherent cells continuously, periodically, or intermittently, without disturbing adherent cells.

118. (New): The method of Claim 117, wherein the human T-cells are cultured for at least 2 days.

119. (New): The method of Claim 117, wherein the culture medium contains at least 1 growth factor which stimulates the proliferation of the human T-cells.

120. (New): The method of Claim 95, wherein the T-cells cultured are antigen specific T-cells.

121. (New): The method of Claim 120, wherein the antigen specific T cells are specific for a viral antigen.

122. (New): The method of Claim 120, wherein the antigen specific T cells are specific for a tumor reactive antigen.

123. (New): The method of Claim 95, wherein the T-cells cultured are cytotoxic T cells.

124. (New): The method of Claim 95, wherein the T-cells cultured are cytokine induced killer cells.

125. (New): The method of Claim 95, wherein the T-cells are CD3+ and CD8+ T-cells.

126. (New): The method of Claim 95, wherein the T-cells are CD3+ and CD4+ T-cells.

127. (New): The method of Claim 95, wherein the T-cells are CD3+ and CD56+ T-cells.

128. (New): The method of Claim 95, wherein the T-cells obtained by culturing have enhanced cytotoxicity and secretion of cytokines relative to T-cells cultured in static and hemi-depletion cultures.

129. (New): The method of Claim 128, wherein the cytokines are IFN- γ , IL-10, TNF- α , GM-CSF and mixtures of these.

130. (New): The method of Claim 95, wherein the liquid culture medium comprises IL-2, IL-7 or both IL-2 and IL-7.

131. (New) The method of Claim 95, wherein the human T-cells are inoculated in the culture medium in a density of from about 5×10^4 to 2×10^6 cells/ml of liquid culture medium and wherein the density of the T-cells after culturing is from about 5×10^6 to 5×10^7 cells/ml.

132. (New) The method of Claim 95, wherein the human T-cells are inoculated in the culture medium in a density of from about 0.16×10^6 to 0.32×10^6 cells/ml of liquid culture medium and wherein the density of the T-cells after culturing is from about 12×10^6 to 32×10^7 cells/ml.